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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,691	03/08/2004	Marc Bellotti	44378/293531 (13131-0331)	6082

23370 7590 09/09/2005

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HC

Office Action Summary	Application No.	Applicant(s)	
	10/796,691	BELLOTTI ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-24 and 73-75* is/are pending in the application.

4a) Of the above claim(s) *25-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-24 and 73-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

This Office action is in response to the amendment filed July 12, 2005. **Claims 1-2, 4-24 and 73-75** are presently pending and under examination.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn.

New Objection(s) and Rejection(s)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-13, 73-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **Claim 1** has been amended to include the following phrase, "obtaining a mixture of high density lipoprotein particles and low density particles from a biological fluid"; however the specification of the present application does not provide written description support for the mentioned phrase. The specification and examples in the specification discuss obtaining HDL particles or LDL particles from blood plasma but there is no mention of a mixture of LDL

and HDL particles that is obtained form biological fluids. It must be also noted that blood plasma is indeed considered to be a biological fluid, but it is not the only biological fluid. The scope of "biological fluid" is considerably larger than blood plasma; therefore by itself blood plasma cannot be considered to be sufficient written description for biological fluids of all kind.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-24, 74 and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Clay et al., 1999.

Claims 1-2, 4-24, 74 and 75 are product by process claims, "[even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). The final product of the process is a particle derivative of at least one form of high-density lipoprotein particle comprising apolipoprotein A-1 and phospholipids wherein the lipid or cholesterol content of the

particle has been lowered. The origin of the product is not presently germane in view of considering the patentability of the product, since patentable weight is given to the final form of the product; therefore the fact that the source of the product in this case appears to be a biological fluid is not considered to be essential; however the fact that the original form of the presently claimed product contained a higher amount of lipids or cholesterol is being considered.Clay et al. teach that Human apoA-I and apoA-II were obtained form plasma from normal volunteers and delipidated (Page 445, column 2, paragraph 2 lines 1 and 11). Clay et al. teach further that aliquots of HDL density fraction, which had been isolated form incubations containing lipid-free apoA-I, lipid free apoA-II, LDL and sodium oleate, were rotated with anti-(apoA-I) Sepharose in order to obtain a pure sample (Page 446, column 2, paragraph 5, lines 1-5).

Clay et al. also teach that most of the apoA-II in human plasma is accommodated in HDL particles containing both apoA-1 and apoA-II (A-I/A-II HDL) and that it was conceived that the process in which A-I HDL and A-II HDL were formed from lipid-free proteins in incubations with sodium oleate and LDL might also result in the formation of A-I/A-II HDL. Clay et al. state that in order to investigate the mentioned hypothesis lipid free apoA-I was mixed with lipid-free apoA-II and incubated at 37 degrees C in the presence of LDL (Page 448, column 1, lines 1-15).

Clay et al. teach further that apoA-I that was recovered in the HDL fraction was present in three main populations of particles; two of the populations had pre-beta 2 mobility and one had pre-beta 1 mobility (Page 448, column 2, lines 4-8).

Clay et al. also disclose a composition containing lipid and cholesterol free apoA-I and apoA-II with phospholipids (Page 450, Table 2).

Clay et al. teach that, as was the case with the A- I HDL described previously and the A-II HDL formed in the present study, mixture of A-I HDL and A-I/A-II HDL contained phospholipids, but only a trace amount of cholesterol esters or triacylglycerol and therefore probably discoidal rather than spherical particles (Page 450, column 2, paragraph 3, lines 16-26).

It is important to point out that clay teaches that it is known that there are 3, subgroups of HDL (AI, AII, and AI/AII) in plasma, consequently applicants product of the invention is also obtained from plasma and contains at least one of the three mentioned subgroups in a delipidated form. Even though Clay et. al have used a different method of obtaining the final product, the final product is reconstituted and exists in an equilibrium that is identical to how the product would behave it its natural environment. It is particularly noted that on page 451, column 2, lines 4-8, Clay et al. have stated that "regardless of the sequence of events, it is apparent that when lipid free apoA-I and lipid free apoA-II are exposed to LDLs, one of the products formed is a population of A-I/A-II HDL. Clay et al. further assert that it has been shown that lipid free apoA-II can recruit lipids from other lipoproteins to form new "lipid HDL, in a similar manner to that previously described for apoA-I, and when both lipid free apolipoproteins are present, a portion of the new HDLs fromed contain both apoA-I and apo-AII; this observation has potential importance in terms of understanding the formation of apolipoprotein-specific HDLs with human plasma (Page 451, column 1, paragraph 3, lines 2-9). It must also be

stated that the applicants have made the submission on the record in the response section of the amendment filed July 12, 2005 that the applicants' product of the invention inherently comprises other components found in natural high density lipoprotein particles such as apolipoprotein A-II (page 4, lines 7-9).

Thus Clay et al. teach all the elements of **Claims 1-2, 4-24, 74 and 75** and these claims are anticipated under 35 USC 102(b).

Claims 1-2, 4-24, 74 and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Durbin et al., 1999.

As mentioned above **Claims 1-2, 4-24, 74 and 75** are product by process claims.

Durbin et al. teach that human apoA-I, apoA-II were prepared from blood plasma purchased form the Champaign county Blood Bank (Page 2294, column 2, lines 9-13)

Durbin et al. teach further that the effect of lipid free apolipoproteins on rHDL structure and particle size distribution was examined by adding lipid free apoA-1 or apo-AII to A-II-POPCrHDL or A-I POPCrHDL, in a molar ratio of 1:1, lipid free apolipoprotein per rHDL particle (Page 2295, column 1, paragraph 3, lines 1-6).

Durbin et al. also teach that lipid free or lipid poor apolipoproteins bind to existing lipoproteins and in particular apoA-I, recruit phospholipids and cholesterol from cell membranes forming pre-beta-1 HDL and in the later process, nascent pre-beta-1 HDL are transformed into discodial pre-beta HDL (Page 2293, column 2, lines 12-15).

Durbin et al. disclose a composition comprising a HDL particle derivative containing lipid free ApoA-I and ApoA-II, phospholipids and HDL (Page 2300, Table 2).

Durbin et al. assert that, lipid free apolipoproteins, by their interaction with nascent and mature HDL particles can markedly influence their reaction with LCAT in one of the key steps in reverse cholesterol transport and also that lipid free apolipoproteins promote the remodeling of HDL to smaller particles, some of which have pre-beta 1 mobility and are expected to very effective acceptors of cholesterol in reverse cholesterol transport (Page 2301, column 1, paragraph 3, lines 1-10).

It is important to not that even though Durbin et al. have not obtained their high density lipoprotein particles in the same manner as the applicants, it has been clearly demonstrated in Fig 8. and Table 2 on page 2300 that the final product is reactive and resembles the product of the invention with regards to its function as an effective acceptor of cholesterol in reverse cholesterol transport.

Thus Durbin et al., 1999 teach all the elements of **Claims 1-2, 4-24, 74 and 75** and these claims are anticipated under 35 USC 102(b).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4-24, 74 and 75 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over **claims 73-78 and 80** of copending Application No. 10996570. Although the conflicting claims are not identical, they are not patentably distinct from each other because **Claims 1-2, 4-24, 74 and 75** of the present application disclose a composition comprising a HDL particle derivative wherein the particle derivative comprises apolipoprotein A-I, apolipoprotein A-II and phospholipids wherein the lipid content or the cholesterol content of the composition has been lowered. Consequently **claims 73-78 and 80** of application 10996570 also disclose a composition comprising a HDL particle derivative wherein the particle derivative comprises apolipoprotein A-I, apolipoprotein A-II and phospholipids wherein the lipid content or the cholesterol content of the composition has been lowered

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

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04-03-05